DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

BLA 103780/5178
BLA 103780/5179

SUPPLEMENT APPROVAL

EMD Serono, Inc.
Attention: Holly Leonard
Associate Director, Global Regulatory Affairs
One Technology Place
Rockland, MA
02370

Dear Ms. Leonard:

Please refer to your Supplemental Biologics License Applications, dated June 17, 2013, received June 18, 2013, and dated June 26, 2013, received June 27, 2013, submitted under section 351(a) of the Public Health Service Act for Rebif (interferon beta-1a) injection.

We acknowledge receipt of your amendments dated November 26, 2013, January 22, 2014, and April 3, 2014.

Supplement 5178, dated June 17, 2013, constituted a complete response to our April 11, 2013, action letter for four "Changes Being Effected" supplemental biologics applications. These "Changes Being Effected" supplemental biologics applications propose the following:

5099	Revision to the adverse reactions section of the package insert to include injection site reactions and cases of pseudo-relapses and revisions to the medication guide related to injection site problems.
5108	Revision to the adverse reactions section of the package insert to include erythema multiforme and Stevens-Johnson syndrome as well as information regarding suicide and hepatic injury in the postmarketing section of the package insert.
5119	Revision to the adverse reactions section of the package insert to include reports of thrombotic thrombocytopenic purpura and hemolytic uremic syndrome, retinal vascular disorders, and convulsive disorders.
5162	Revision to the adverse reactions section of the package insert to include systemic lupus erythematosus, autoimmune hepatitis, and pancytopenia.

Supplement 5179, a "Prior Approval" supplemental biologics application, proposes revised labeling for Rebif in accordance with the Physicians' Labeling Rule (PLR).

APPROVAL & LABELING

We have completed our review of these supplemental applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, via the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 601.14(b)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical to the enclosed labeling (text for the package insert and Medication Guide) and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements. Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this BLA, including pending "Changes Being Effected" (CBE) supplements, for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 601.12(f)] in MS Word format that includes the changes approved in this supplemental application.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your application, you are exempt from this requirement.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 601.12(f)(4), you must submit final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf. Information and Instructions for completing the form can be found at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved BLA (in 21 CFR 600.80 and in 21 CFR 600.81).

If you have any questions, please contact the Regulatory Project Manager, LCDR Hamet Touré, PharmD MPH, at (301) 796-7534.

Sincerely,

{See appended electronic signature page}

Billy Dunn, MD
Acting Division Director
Division of Neurology Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ENCLOSURE:
Content of Labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

WILLIAM H Dunn
04/24/2014